Treatment of obesity - A review through the eyes of a primary care physician

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ABSTRACT

Aim: To provide primary care physicians with a comprehensive knowledge of non-pharmacological, pharmacological and surgical treatments for obesity, increasing the effectiveness of obesity treatment in primary care settings.

Methods: Pubmed and Google Scholar databases, magazine Practical Medicine and WHO page were searched using the keywords: "obesity", "pharmacological treatment of obesity", "non-pharmacological treatment of obesity", "bariatric surgery". We then analyzed a selection of material. Non-pharmacological methods, such as diet, physical activity and psychological support, are the cornerstone of obesity treatment.

Results: Pharmacological treatment includes combinations of naltrexone and bupropion, liraglutide, semaglutide and orlistat, used when non-pharmacological interventions do not have the desired effect. Bariatric surgery, which is effective for severe obesity, includes procedures such as LSG and LRYGB, which are highly effective in reducing weight and treating comorbidities. Conclusion: Successful obesity treatment requires a multifaceted approach combining non-pharmacological, pharmacological, and surgical methods. Semaglutide, the most effective drug, aids weight loss and improves metabolic parameters. Bariatric surgery is most effective for grade 3 obesity but necessitates careful patient selection and post-surgery dietary adherence Keyword: Obesity; overweight; family doctor; primary care physician

INTRODUCTION

Obesity is a chronic disease characterized by excessive accumulation of fat tissue, classified in the ICD-10 classification as E66.0. It is one of the major health challenges of the 21st century. Obesity is caused by a prolonged energy imbalance, where the amount of energy consumed exceeds the amount of energy expended. Sleep debt causes an increase in appetite and therefore the consumption of more energy. Another factor causing weight gain is certain medications, e.g. psychotropic medication, diabetic treatments, antihypertensive, steroid hormones and contraceptives, antihistamines, and protease inhibitors¹. The National Center for Nutritional Education cites the following as main causes of this condition: lack of physical activity, lack of awareness of the caloric content of consumed products, irregular meal consumption, consumption of sweetened drinks, and fried foods².

To diagnose this disease and to determine its degree and type, anthropometric measurements are conducted. Body weight, height, and waist circumference need to be measured. Obesity is classified based on BMI measurements, for which:

- Normal weight: 18.5-24.9
- Overweight: 25.0-29.9
- Class 1 Obesity 30.0-34.9
- Class 2 Obesity: 35.0-39.9 .
- Class 3 Obesity 40.0 and above

Visceral obesity, which is associated with the highest risk of complications, is diagnosed if the waist circumference in

Europeans is at least 94 cm in men and at least 80 cm in women. The main complications of obesity are:

- Type 2 diabetes
- Hypertension
- Cardiovascular diseases
- Sleep apnea syndrome

- Obesity hypoventilation syndrome •
- Joint diseases requiring surgical treatment
- Non-alcoholic steatohepatitis .
- Non-alcoholic fatty liver disease
- Hyperlipidemia
- Infertility in women, including that associated with polycystic ovary syndrome³.

Obesity is a condition with multidimensional consequences, requiring a holistic approach in diagnosis and treatment. Reducing body weight in obese individuals by 5-7% in patients with prediabetes and other cardiovascular risk factors can effectively improve glycemic control, blood pressure, and blood lipid levels, and reduce the progression of type 2 diabetes⁴. Prevention and treatment of this disease are crucial to avoid its complications, which can overload the healthcare system and are very costly to treat.

Obesity is currently one of the most serious health problems in the world, reaching epidemic proportions, with the number of affected individuals steadily increasing. According to the WHO, in 2022, every eighth adult was obese, and overweight affected 43% of all adults worldwide⁵. From 1990 to 2022, obesity among children and adolescents aged 5 to 19 years globally increased fourfold⁵. Over the past 50 years, the number of people with obesity has nearly tripled, and it is currently estimated that 13% of the global adult population is affected by this disease. There is an observed increase in the incidence of obesity in progressively younger age groups⁶. A WHO report published in 2022 states that in Europe, nearly 60% of adults are obese or overweight, making it the fourth most prevalent risk factor for non-communicable diseases. This problem affects nearly 30% of European children (29% of boys and 27% of girls)⁷. Worldwide, overweight and obesity affect 10% of children and adolescents. According to WHO predictions, by 2025 there will be 177 million children aged 5-17 with overweight and 91 million who will be obese⁸. Studies report that 80% of obese adolescents remain affected by this problem into adulthood⁹. The increase in the number of obese individuals contributes to the rise in obesity-related diseases. According to WHO, by 2025, approximately 12 million children in Europe will have impaired glucose tolerance, 4 million will have type 2 diabetes, and 27 million will have hypertension⁸.

The aim of this study is to provide primary care physicians with comprehensive knowledge about the available methods of treating obesity, allowing for more effective treatment of this condition

Non-Pharmacological Methods of Treating Obesity: The cornerstone of treating obesity is dietary management. The Society for the Treatment of Obesity recommends a diet that provides 500-600 kcal less than the patient's daily energy requirement. Energy requirements can be calculated in a clinical setting using specialized online calculators. The patient's diet must be properly balanced to avoid nutrient deficiencies. The patient should consume 3-5 meals per day, including an overnight fasting period. The diet should provide 15-18% of energy from protein, 35-60% from carbohydrates, and 20-45% from fats.

Patients should be instructed at primary care clinics on the principles of healthy eating and the need to avoid highly processed foods (which increase the risk of developing type 2 diabetes by 74%), as well as foods high in sugar and animal fats. Instead, they should consume whole grain products, vegetables, nuts, and low-fat dairy. Fiber has a beneficial effect on glycemic control, post-meal satiety, and gastrointestinal function; therefore, patients should consume 18-38g of fiber daily (including 5-10g of soluble fiber).

The Mediterranean and DASH diets have proven effective in reducing the development of obesity. Long-term adherence to the Mediterranean diet, with a caloric deficit and regular physical activity, leads to weight loss, a 19-23% reduction in the incidence of type 2 diabetes, and improved insulin sensitivity. Meanwhile, vegetarian and vegan diets reduce the risk of developing diabetes by 47-78%, lower the HOMA-IR insulin resistance index, and, when maintaining a caloric deficit, yield good results in treating obesity and its metabolic complications^{4,10}.

Physical activity is a crucial element of comprehensive obesity treatment. According to the American Heart Association, lifestyle changes can be more effective in reducing visceral fat than pharmacological treatment. A reduction of visceral fat by up to 6% can occur without weight loss, which is associated with an increase in lean body mass. Aerobic exercises are most beneficial for reducing visceral fat, and performing them for 150 minutes per week is sufficient for weight loss¹⁷. Aerobic exercises should engage larger muscle groups. For beginners, these exercises should be performed at an intensity of 40-60% VO2 max, and for advanced individuals at 60-70% VO2 max. Initially, it is recommended to perform aerobic exercises 2-3 times a week for 15-30 minutes (gradually increasing to 60 minutes daily), and later increasing the frequency to 4-5 times weekly. In the 3rd or 4th week of exercise, after aerobic workouts, 20-30 minutes of resistance exercises using light weights can be added. The number of repetitions should be 15-20, starting with one set and increasing to four sets, with a 30-60 second break between sets, and repeating the training every 48 hours¹²

Obese individuals are more likely to struggle with anxiety and depressive disorders compared to those with normal body weight. More than half of the patients classified for bariatric treatment suffer from at least one of the following disorders: social phobia, hypochondria, obsessive-compulsive disorders, depression, and somatization disorders. Eating disorders are also commonly observed among those classified for bariatric surgery, affecting approximately 30 to 50% of obese individuals (compared to 2-5% of the general population), and the night eating syndrome, which affects obese individuals five times more frequently¹³. Therefore, providing psychological and psychiatric care to patients helps in the fight against obesity.

Pharmacological Methods of Treating Obesity: Pharmacological methods for treating obesity should be introduced when dietary and behavioral treatments have not achieved significant weight reduction and therapeutic goals, and the following criteria are met:

- Adults with a BMI ≥30 kg/m²
- Adults with a BMI of 27-29.9 kg/m² and at least one weightrelated condition, such as carbohydrate metabolism disorders (prediabetes or diabetes), hypertension, dyslipidemia, or obstructive sleep apnea
- Adolescents aged 12 and older, weighing more than 60 kg, with obesity diagnosed according to international cut-off points (as per the International Obesity Task Force criteria)⁴.

Combination preparation of naltrexone and bupropion: Naltrexone is a drug used to treat alcohol and opioid dependence¹⁴. Bupropion, on the other hand, is a neuronal reuptake inhibitor of norepinephrine and dopamine used to treat nicotine dependence and episodes of major depression¹⁵ The combination is elaborated about the mechanism of action of leptin, which acts to stimulate proopiomelanocortin neurons (POMC) in the melanocortical system. Stimulated POMC signalling in the hypothalamus, responsible for reducing food intake, and increasing energy expenditure is inhibited by endogenous feedback. Bupropion stimulates POMC neurons, whereas naltrexone blocks endogenous feedback inhibiting POMC activity¹⁶ One tablet contains 8 mg of naltrexone hydrochloride, equivalent to 7.2 mg of naltrexone and 90 mg of bupropion hydrochloride, equivalent to 78mg of bupropion. This medicine is best taken with a meal. Treatment should be started with 1 tablet in the morning for 7 days. then 1 tablet in the morning and 1 tablet in the evening for 7 days, in the 3rd week of use 2 tablets in the morning and 1 tablet in the evening, in the 4th week and following weeks 2 tablets in the morning and 2 tablets in the evening should be used. The maximum dose is 4 tablets per day. If, after 16 weeks of treatment, body weight is not reduced by 5% of the initial weight, treatment should be discontinued. Once a year, the need for this medication should be reviewed¹⁷. The drug is contraindicated in patients with uncompensated hypertension, epilepsy, CNS tumours, severe hepatic impairment, end-stage renal failure or severe renal impairment, bipolar affective disorder, opioid dependence⁴. Combination preparation of naltrexone and bupropion side effects include nausea, udder, constipation, headache and dizziness, insomnia, dry mouth¹⁸

Liraglutide: Liraglutide is an analogue of human glucagon-like peptide 1 (GLP-1), 97% homologous to human GLP-1, differing from human GLP-1 by only two amino acids. Due to its binding to albumin and greater stability against dipeptidylpeptidase 4 and neutral endopeptidase, liraglutide is more stable than human GLP-1, making it suitable for subcutaneous once-daily administration. Liraglutide activates the GLP-1 receptor in the brain, resulting in increased satiety signals and decreased hunger signals, the mechanism of this action is not explained. This drug may cause nausea, vomiting, diarrhoea and constipation^{4,19}. Liraglutide 1.8 mg used to treat type 2 diabetes significantly reduces the risk of cardiovascular death, myocardial infarction and non-fatal stroke. In contrast, use of liraglutide 3 mg is associated with an increase in heart rate and a reduction in systolic blood pressure¹¹. A study was conducted among adolescents and a reduction in BMI of at least 5% after use for 56 weeks of liraglutide was observed in 43% of subjects, compared with only 19% in the placebo group, while a reduction in BMI of at least 10% was observed in 26% of those who used the drug and 8% of those in the control group²

Semaglutide: Semaglutide is the most effective drug for weight loss²¹. This drug is a GLP-1 analogue, 94% homologous to human GLP-1. It activates the GLP-1 receptor. Semaglutide regulates insulin and glucagon secretion in a glucose-dependent manner and reduces fasting and postprandial glucose levels. Semaglutide inhibits cravings (including for high-fat foods), has a beneficial effect on plasma lipid concentrations, reduces inflammation and lowers systolic blood pressure. Animal studies have proven to reduce atherosclerotic plaque development and inflammation, thus preventing the development of atherosclerosis²².

It is the most effective drug for weight loss. A study was conducted in which 2.4 mg of semaglutide was used for 104 weeks. 68% of patients in the study group achieved a weight loss of ≥5% and only 21% in the placebo group, by ≥ 10% 44% using the drug and 7% in the placebo group, a weight loss of ≥15% was achieved by 23% in the study group and 2% in the placebo group²³

This drug is administered 1 time per week, subcutaneously in the abdomen, thigh, arm, at any time of the day and independent of meals. For adults, the initial dose is 0.25mg/week for 4 weeks, then this is increased to 0.5mg/week at week 5-8, then 1 mg/week at week 9-12, 1.7mg/week at week 13-16 and from week 17 onwards 2.4mg/week is used²².

Patients taking semaglutide should have their heart rate monitored, as the drug may cause an increase in heart rate²¹ Adverse effects very common with this drug include headache, vomiting, diarrhoea, constipation, nausea, headache and fatigue²².

A study comparing the efficacy in weight loss of semaglutide with liraglutide was conducted. The study was conducted for 68 weeks and the therapeutic doses of the drugs (semaglutide 2.4 mg once a week, and liraglutide 3 mg once a day) were used in both groups. A greater reduction in body weight and a lower frequency of treatment discontinuation were demonstrated in semaglutide users. On average, patients using semaglutide reduced their body weight by 15.8% and liraglutide by 6.4%²

Orlistat: Orlistat is a pancreatic lipase inhibitor, which results in inhibition of the breakdown of triglycerides into fatty acids. Its use at a therapeutic dose of 120 mg 3 times daily reduces the absorption of ingested fats by approximately 30%, which contributes to a caloric deficit²⁵. The reduction in fat absorption results in a reduction in the absorption of fat-soluble vitamins, so multivitamin preparations should be supplemented, a minimum of two hours after ingestion of orlistat. On average, patients lose about 5.6kg in the first six months of use (in comparison, the placebo group lost about 2.4kg). In addition, Orlistat has a beneficial effect on reducing BMI, total cholesterol, low-density lipoproteins and waist circumference²⁶. This practical drug is not absorbed in the gastrointestinal tract (1 to 3% of the drug administered orally) its side effects, i.e. abdominal discomfort, flatulence and fatty diarrhoea, are due to its effect on fat absorption. In order to reduce these, consumption of fat-rich meals should be avoided and gastrointestinal symptoms decrease with longer treatment²⁷. Orlistat impairs the absorption and thus the normal action of some drugs e.g. amiodarone. It may reduce the absorption of lipophilic antiepileptic drugs, i.e. lamotrigine, valproate, vigabatrin and gabapentin, so their levels should be monitored. Levothyroxine and orlistat should be taken at a minimum interval of 4h to avoid decreased absorption. Concomitant use of orlistat, which reduces vitamin K absorption, and warfarin may prolong prothrombin time and INR, so continuous monitoring of these parameters is required²⁶. Orlistat is the drug of third choice in the pharmacological treatment of obesity²

Bariatric surgery Bariatric surgery is currently the only method with proven long-term efficacy in patients with the most advanced obesity. Surgical treatment of obese patients, should be part of an intersystemic management including nutritional education, psychological support, physical improvement and pharmacological treatment⁴. Most patients achieve more than 50% of their excess weight loss (the difference between the current weight and the ideal weight for the patient) in the first year after surgery. In the follow-up, which lasted more than one year, it was proven that weight reduction or further weight maintenance depends on changes in lifestyle and eating habits. Unfortunately, about 15-20% of patients require re-operation³.

Qualification of a patient for bariatric surgery should include: indication of the degree of obesity by calculating the BMI taking into account the patient's current and highest weight, the presence of complications of obesity and contraindications to bariatric

surgery, determination of biological age in the case of patients over 65⁴. Surgery may also be considered in patients:

- With grade III obesity 1.
- With grade II obesity if: 2.
 - Treatment will result in improvement in diabetes-related disease
 - Are important social, psychological indications
 - Obesity disqualifies from surgical treatment in the course of other diseases
- With grade I obesity and type 2 diabetes when hyperglycaemia persists and therapeutic goals are not 3. achieved despite intensive treatment With grade III obesity Absolute contraindications to bariatric surgery are:
- Incurable diseases leading to cachexia
- 1. Diseases that pose an immediate threat to life 2
- 3. Endocrine diseases underlying obesity
- Severe coagulation disorders 4
- Lack of cooperation from the patient or lack of acceptance of 5. the effect of the treatment due to
- 6 Inability to have regular post-operative visits
- 12 months prior to planned pregnancy, pregnancy and 7. breastfeeding
- 8. Lack of consent of the patient
- Conditions preventing independent living when family or 9 social care is unable to provide adequate long-term supervision²⁹

Bariatric surgery is very safe. The perioperative mortality rate is 0.03-0.2%. In the perioperative period, the most common complications are bleeding into the peritoneal cavity or gastrointestinal tract, gastrointestinal leakage in the anastomotic line. gastrointestinal obstruction, gastrointestinal leakage, infections and thromboembolic complications. Distant complications are nutritional deficiencies, anaemia (resulting from patients' non-compliance with dietary and supplementation recommendations) postoperative hernias and cholelithiasis³.

The most commonly performed bariatric procedure is laparoscopic sleeve gastrectomy (LSG), which involves the removal of a significant portion of the stomach, reducing its volume. This procedure is very effective, the percentage loss of excess BMI averaging 24.4% weight loss 10 years after surgery. LSG is effective in helping to treat type 2 diabetes and hypertension, the remission rate after surgery being 45.6% for type 2 diabetes and 41.4% for hypertension respectively³⁰. In patients with non-alcoholic fatty liver disease (NAFLD) and morbid obesity, improvements in laboratory parameters, i.e. AST,ALT,GGT, LDH, and a reduction in the liver fibrosis index were observed one year after surgery³¹.

Fig.1 Laparoscopic sleeve gastrectomy³²



Laparoscopic gastric exclusion surgery with Roux loop (LRYGBP) is the most commonly performed bariatric surgery after LSG (accounting for 59% of all bariatric procedures in 2019). LRYGB in 2019 accounted for 17.8% of all bariatric surgeries³². It involves separating the stomach using a cutting and sewing stapler into a mini-gastric pouch (the proximal part with a volume of 20-100 cm3, the so-called gastric pouch) and a distal part, which is excluded from the passage of food content. The surgeon then

produces a Roux-en-Y loop consisting of 3 elements: a digestive loop, an enzymatic loop and a common or digestive loop. Later, the Roux loop is anastomosed to the proximal part of the stomach. It combines the restriction of ingested food and the reduction of its absorption in the body. This operation is particularly effective in the treatment of metabolic syndrome, especially diabetes. Studies show that LRYGBP can lead to diabetes remission in up to 80% of patients, with a further 10% experiencing a significant reduction in insulin requirements³³. Patients following LRYGBP, through reduced nutrient absorption, are at risk of developing vitamin and mineral deficiencies, especially vitamin B12, and therefore its levels must be monitored and any deficiencies supplemented¹³. Probiotic supplementation is very important, as it has been shown to reduce food addiction and the frequency of overeating episodes, and to benefit patients' mental health³⁴.





There was a study comparing LSG and LRYGB, both procedures had the same efficacy in terms of weight loss and improvement in type 2 diabetes control. However, LSG has a lower incidence of early postoperative complications (obstruction, intraabdominal abscess formation, pleural abscess, leakage at the gastrojejunostomy site) and a higher incidence of oesophageal reflux disease, as well as a lower need for reoperation. In contrast, patients after LRYGB were more likely to suffer from postprandial syndrome (early, when vomiting, bloating, diarrhoea, dizziness, palpitations, and late in which hypoglycaemia occurs). Patients who underwent LRYGB had better outcomes in dyslipidaemia, hypertension and gastro-oesophageal reflux disease^{3,35}. Aboth of these procedures, patients should supplement orally with 400-800 µg of folic acid. LSG and LRYGB cause a reduction in gastric acid secretion, resulting in a reduction in the availability of reduced forms of iron, which are better absorbed by the body, so iron should be closely monitored and supplemented after these procedures¹³

Bariatric surgery is very effective, with the majority of patients losing more than 50% of their excess body weight (i.e. the difference between the patient's current weight and the ideal weight for a given height and gender) in the first year after surgery. Weight maintenance and reduction one year after surgery depends mainly on the patient's own eating habits and physical activity. Subsequent surgical intervention for weight reduction requires about 15-20% of operated patients³. Long-term follow-up has shown improved patient health, not only due to the loss of excess body weight but also a reduction in the severity and remission of obesity-related diseases, a reduction in cardiovascular risk, and improved mental health. Many patients who were unable to work due to their obesity are taking up employment after surgery³⁶.

An adequate diet is a very important component of the success of bariatric surgery. The composition of the diet should depend on the type of operation and the time elapsed since the operation. It is important that the patient eats an adequate amount of food per day, divided into at least 4 meals, every 3-4 hours. During the first few days, the diet should be liquid and semi-liquid, and over time the diet should be expanded to include solid foods. The diet should be high in protein and contain foods rich in nutrients and B vitamins⁴.

SUMMARY

Obesity is a major global health problem, the number of people affected is steadily increasing and there is an increase in incidence in younger age groups. In 2022, 13% of adults worldwide were obese and 43% were overweight. GPs play a key role in the fight against obesity by educating patients about healthy lifestyles and the risks of obesity. This article describes a comprehensive approach to the treatment of obesity, emphasising non-pharmacological methods such as dietary changes, increased physical activity and lifestyle modifications.

A key role in the treatment of obesity is diet, which should be balanced and result in energy deficits. Physical activity, especially aerobic and strength training, is an important element in the reduction of fat, especially visceral fat, and to maintain good health. Psychological support is also essential due to the higher prevalence of mental health problems among obese people.

When non-pharmacological methods are insufficient, pharmacological treatment can be used. Available drugs include naltrexone with bupropion, liraglutide, semaglutide and orlistat. Each drug has specific indications, mechanisms of action and potential side effects that clinicians should be aware of. Bariatric surgery is the most effective long-term treatment for severe obesity. LSG and LRYGB are the most commonly performed surgical procedures. They require a multidisciplinary approach, including nutritional education and psychological support. Despite the risk of complications, these surgeries lead to significant weight loss and improvement of obesity-related conditions.

This article aims to provide primary care physicians with a comprehensive understanding of obesity management, enabling them to provide effective treatment and appropriate referrals for surgical interventions when necessary. A holistic approach is key to managing obesity and reducing its associated health risks.

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- 1. Conception and design of or acquisition of data or analysis and interpretation of data.
- Drafting the manuscript or revising it critically for important intellectual content.
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